



# Resting connectivity predicts task activation in pre-surgical populations



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## ABSTRACT

Injury and disease affect neural processing and increase individual variations in patients when compared with healthy controls. Understanding this increased variability is critical for identifying the anatomical location of eloquent brain areas for pre-surgical planning. Here we show that precise and reliable language maps can be inferred in patient populations from resting scans of idle brain activity. We trained a predictive model on pairs of resting-state and task-evoked data and tested it to predict activation of unseen patients and healthy controls based on their resting-state data alone. A well-validated language task (category fluency) was used in acquiring the task-evoked fMRI data. Although patients showed greater variation in their actual language maps, our models successfully learned variations in both patient and control responses from the individual resting-connectivity features. Importantly, we further demonstrate that a model trained exclusively on the more-homogenous control group can be used to predict task activations in patients. These results are the first to show that resting connectivity robustly predicts individual differences in neural response in cases of pathological variability.

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## 1. Introduction

When presented with the same task, each person's brain tends to respond in an idiosyncratic way (Penfield and Roberts, 1959; Ojemann et al., 1989). From the point of view of task-based fMRI, these *individual differences* can be seen as distinct spatial patterns of neural activation. Although there are strong similarities between individual brains, which allow for group studies to be carried out, group averages lack the specificity of single-subject fMRI. This is critical for the use of fMRI in pre-surgical planning where the degree of individual variability is typically higher in patients compared to non-surgical controls. Single-subject task-based fMRI therefore provides a valuable tool for the identification of neural tissues associated with key functions such as language processing (Binder et al., 1997; Price, 2012), particularly as the exact location and extent of higher-order cortical areas cannot, in general, be determined from gross anatomy (Fischl et al., 2008). One specific challenge is that task-based fMRI requires subjects to perform experimental tasks. However, not all pre-surgical patients are able to perform these tasks—for reasons that range from patient compliance or fatigue, to the ability to perform or even comprehend the task instructions. Furthermore, the choice of task can be limited by constraints on scan time. For patients who cannot perform the relevant task, a 'task-free'

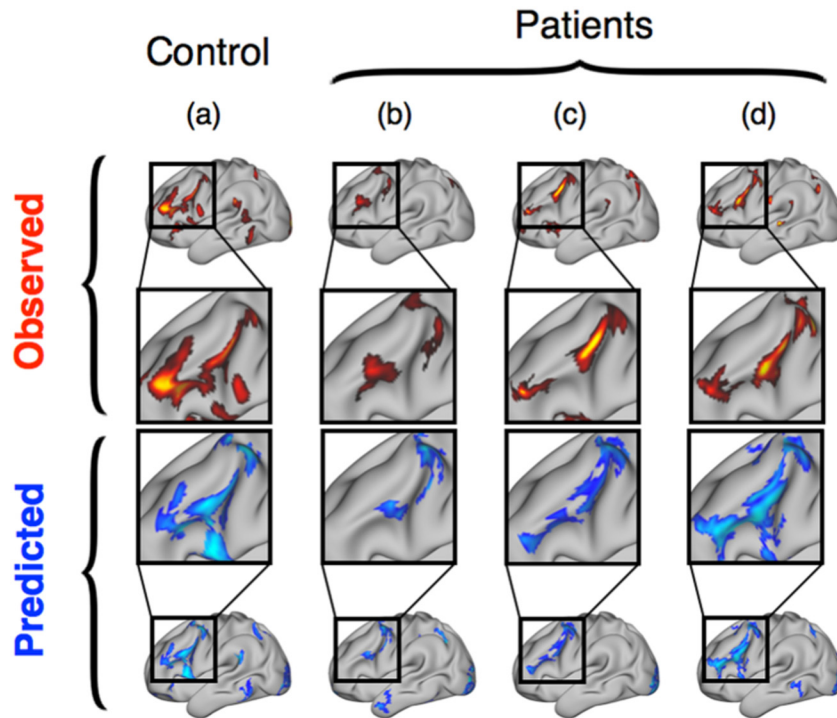
method for mapping brain functions would therefore fill an important gap. In this paper, we ask whether individual variation in activation maps can be predicted for a clinically-relevant language task in pre-surgical patients, using only resting-state fMRI and with no explicit experimental task.

We acquired resting-state and task-evoked fMRI from 71 pre-surgical patients and 32 healthy controls (103 subjects total). The pre-surgical patients had been diagnosed with conditions that represent potential use cases: operable brain tumours, temporal lobe epilepsy, and vascular lesions (specifically, arteriovenous malformations and cavernomas). We acquired task-based fMRI to infer individual task activation maps which were then used to both develop/train and evaluate our model predictions. For the task we used *category fluency*, which is known to activate language-processing areas in the inferior frontal cortex using the contrast [category fluency > fixation baseline] (Paulesu et al., 1997; Costafreda et al., 2006). Healthy volunteer subjects were included in the study to compare the variability of task activity with that of patients, and to compare within-group and between-group predictions. The predictions were produced using a supervised approach (see [Methods](#)). Briefly, the resting-state data were pre-processed into individual subjects' resting-connectivity features, which were then used to train a set of regression models to predict whole-brain task activation maps. This allowed us to produce, from their resting-connectivity features alone, the unseen test subjects' *predicted* task activation maps (Fig. 1).

In prior work, we applied this method to predict task activation maps from resting-connectivity features using healthy control data

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**Fig. 1.** Individual task-contrasts can be predicted from connectivity measures derived from resting-state fMRI. Above: observed task-contrasts (red) for the category-fluency task in four subjects (three patients). Below: predicted task-contrasts (blue) generated using each subject’s resting scan (results from the leave-one-out analysis). Predictions best resemble their paired observations both in healthy and in pathological cases. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

from the Human Connectome Project (Tavor et al., 2016). In that paper, we were able to predict high-fidelity task-activation maps across a wide range of task domains. Important questions however remained unanswered, the most critical being whether our approach could be usefully applied in a clinical setting, given shorter, lower quality data sets and given greater individual variability in patients than in controls. These questions are tackled in the present paper; in addition, we explore the possibility of training a single model on data from healthy controls alone, and then using the model to predict each patient’s task activity. This ‘transfer-learning’ would make it possible, in theory, to predict activity for additional task domains without the need to acquire task-based fMRI training data in patients, potentially opening the doors to a novel and powerful approach to pre-surgical mapping.

**2. Materials and methods**

**2.1. Subjects**

All subjects gave informed consent prior to participating in the study, which was approved by the London Surrey Borders Research Ethics committee.

We report data from 103 subjects: 71 patients and 32 healthy controls. The patients underwent language mapping as part of the study and no patients recruited were excluded from our analyses. Patients presented with pathology in frontal and temporal lobes and were being considered for neurosurgery. The pathologies were: temporal-lobe epilepsy (TLE), brain tumour (TUM), cavernoma (CAV), arteriovenous malformation (AVM), and focal cortical dysplasia (FCD). Because there were relatively few cases of CAV, AVM, and FCD, we combined these into one ‘other’ group (n = 9). The healthy controls (CON) were selected to match the distribution of sex, age, and handedness in the patient group. All subjects had normal or corrected-to-normal vision. This was important as the experiment required subjects to read task instructions from a visual prompt.

In addition to information on sex, age, and handedness, a subset of patients (n = 33) further participated in an intracarotid sodium

amobarbital procedure (‘Wada test’). Another subset of 51 patients provided out-of-scanner behaviour scores for the category fluency task (see Table 1).

**2.2. In-scanner behaviour**

Subjects performed a (covert) category fluency task in scanner. This involved subjects receiving semantic categories as cues before imagining as many nouns in that category as possible. The categories presented were ANIMALS, TOOLS, COUNTRIES, VEHICLES, and FRUITS. Categories were presented as written words on a screen viewable in-scanner. Before beginning the experiment, subjects were instructed to respond covertly, that

**Table 1**

Subject details. Thirty-two of 103 subjects were healthy controls (CON). The remaining 71 represented five neurosurgical conditions: temporal lobe epilepsy (TLE); brain tumour (TUM); cavernoma (CAV); arteriovenous malformation (AVM); and focal cortical dysplasia (FCD). Wada test results are expressed as a real number ranging from -1 (right-hemisphere dominant) to 1 (left-hemisphere dominant). Fluency results reflect the total number of VEGETABLES the subjects named overtly, out-of-scanner in 1 min.

|             | Subject group |         |         |        |        |        |
|-------------|---------------|---------|---------|--------|--------|--------|
|             | CON           | TLE     | TUM     | CAV    | AVM    | FCD    |
| n           | 32            | 42      | 20      | 5      | 3      | 1      |
| Sex         | 17 male       | 20 male | 10 male | 1 male | 2 male | 0 male |
| Age:        |               |         |         |        |        |        |
| Range       | 19–48         | 16–60   | 14–65   | 30–59  | 20–32  | 17–17  |
| Mean        | 32            | 35      | 40      | 44     | 28     | 17     |
| Handedness: |               |         |         |        |        |        |
| right       | 27            | 37      | 19      | 4      | 1      | 1      |
| left        | 4             | 5       | 1       | 1      | 0      | 0      |
| both        | 1             | 0       | 0       | 0      | 2      | 0      |
| Wada:       |               |         |         |        |        |        |
| n           | –             | 29      | 3       | 1      | –      | –      |
| Mean        | –             | 0.6     | 0.7     | 1      | –      | –      |
| Fluency:    |               |         |         |        |        |        |
| n           | –             | 41      | 10      | –      | –      | –      |
| Mean        | –             | 20      | 20      | –      | –      | –      |
| R0061nge    | –             | 8–44    | 9–28    | –      | –      | –      |

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